ABSTRACT

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Title of a diploma work: Induction and inhibition of acenaphthenol dehydrogenase

Breast cancer belongs to hormone-dependent tumours. Apart from lifetime exposure to estrogens, the volume of female active sex hormones in breast tissue also plays a big part in the development of this disease. One of mechanisms regulating concentration of estrogens in the target tissue at the pre-receptor level is their interconversion from inactive estron to its active form, 17β-estradiol enzymes from the aldo-ketoreduktas 1C (AKR1C) subfamily. On the basis of specific substrates, inductive and inhibitive studies, enzymes involved in the conversion of individual hormones can be characterized. Relatively specific substrate for AKR1C is acenaphthenol (AcNOH). However, due to the fact that in a multi-enzyme model system the involvement of other enzymes in the reaction cannot be excluded, the enzymes which take part in conversion of acenaphthenol labeled "acenaphtenol dehydrogenase" (AND). The Aim of my diploma paper is to spectrofluorimetrically determine the activity of AND in cytosole taken from breast tumorous line MCF-7 and in cytosole taken from rat liver tissue and to monitor the modulation of AND's activity with cytostatics doxorubicin (DOX) and oracin (ORA). Short-term (48 hrs.) exposure of MCF-7 cells to non-toxic concentrations of DOX or ORA led to a slight increase of specific activity of AND in comparison with control. The activity of AND in rat liver after p.o. administration of ORA (30mg/kg) was statistically increased in comparison with control. The inhibition studies have proved significant inhibition effect of both DOX and ORA on AND's activity in cytosole of MCF-7 cells. Both substances showed greater inhibitory effect than α-methylcinnamic acid (model inhibitor AND) and to significantly decrease the activity of AND, concentration 100x lower than the concentration of substrate used (AcNOH) was enough. The inhibitory effect of DOX and ORA on the activity of AKR1C enzymes could be one of the mechanisms of cytostatical effect of these substances in hormone-dependent tumours.